Proton Observed Phosphor Editing (POPE) brings hope for in vivo detection of phospholipid metabolites

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Introduction

Preclinical models have shown that the ratio of different phospholipid-metabolites can predict the outcome of cancer treatments[1]. Phosphocholine (PC), phosphoethanolamine (PE) and their respective glycerol compounds (GPC, GPE) can be distinctively detected with ^{31}P MRS in vivo: however, the detection sensitivity is low, hindering translation to clinical use. While ^{1}H to ^{31}P polarization transfer, multi-echo acquisitions and ultra-high field have been shown to improve the signal-to-noise ratio (SNR) in ^{31}P MRS[2], detection via ^{1}H MRS would increase sensitivity even more. Despite the complex spin systems of the phospholipid metabolites, the ^{1}H signals of these compounds are overlapped. Here we demonstrate that selective refocusing of the ^{31}P spins can provide distinct detection of PC, PE, GPC and GPE with ^{1}H MRS. Equally importantly, at 7T we show that the interpulse timings of a sLASER sequence can be set to match their full signal at the optimal ^{31}P TE, providing uncompromised ^{1}H SNR of these compounds. Validated by phantom measurements, and illustrated in the human brain, we show that proton observed phosphorus excited (POPE) provides a 2.8 fold increased SNR per square root time compared to ^{31}P MRS with Ernst angle excitation.

Methods

Inter-pulse timings of an sLASER sequence were optimized using quantum mechanical simulations of the spin systems. Small spherical phantoms with highly concentrated PC, PE, and GPC solutions were positioned in a double tuned breast coil to ensure equally uniform excitations. Full or selective adiabatic refocusing was set for the phosphomonoesters (PME: PC+PE) and diesters (GPC+GPE). An ultrathin quadrature ^{31}P surface coil, interfaced to a Philips 7T system, was designed with 8 ^{1}H traps to fit inside a 16ch ^{1}H receiver headcoil, used for POPE detection in the human brain of a healthy volunteer (TR=3.5s, 256 avg, (4cm)^3).

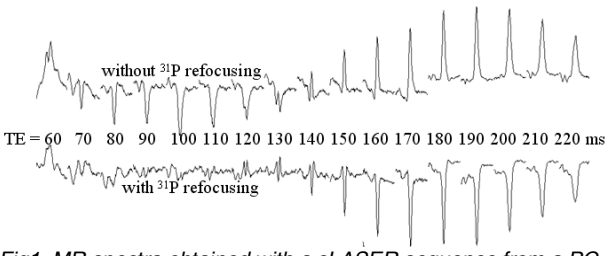

Fig1. MR spectra obtained with a sLASER sequence from a PC phantom either with (bottom) or without (top) ^{31}P refocusing. At TE = 190 ms, the optimal TE for ^{1}H matches the optimal TE for ^{31}P resulting in maximized SNR in the subtracted POPE spectra.

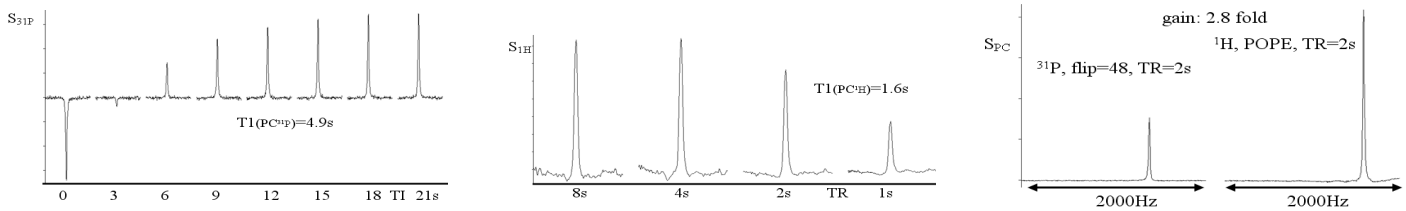

Fig2. Using inversion recovery to estimate the T1 of the ^{31}P spins (left) and progressive saturation for the ^{1}H spins (middle) optimal flip angles for both ^{31}P and ^{1}H could be set resulting in a gain of 2.8 fold in SNR per unit of time (right).

Results

Interpulse timings of the sLASER were set for full absorptive signal detection of the spins of PE, PC, GPE, and GPC (Fig 1). Based on T1 measurements, the sLASER POPE sequence provides a 2.8 fold increased SNR per square root time compared to optimized ^{31}P MRS with Ernst angle excitation (Fig 2). Using the selective refocusing pulses, distinct detection of these metabolites is feasible with ^{1}H MRS with POPE (Fig 3). Merged in an ^{1}H optimized imaging setup, POPE reveals high quality detection in the human brain of PE, PC, GPE and GPC (Fig3).

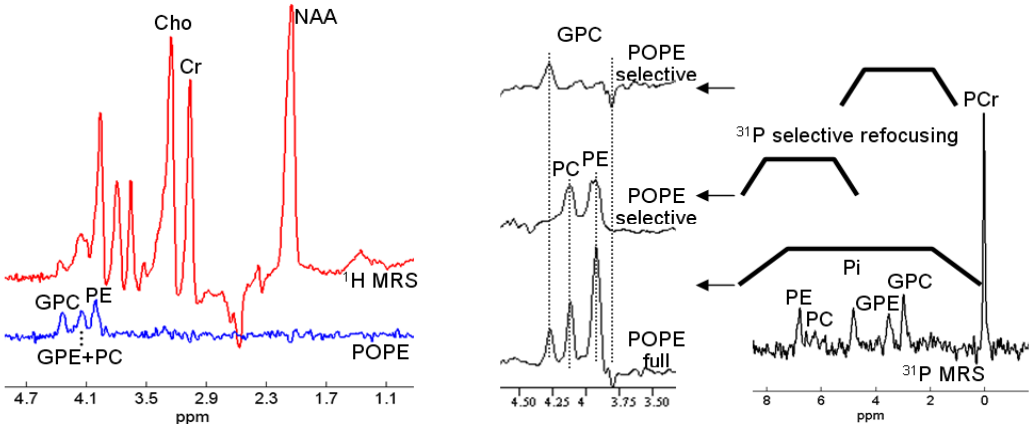

Fig3. left: ^{1}H MR spectra obtained from the human brain using sLASER volume selection with and without full ^{31}P refocusing. Note the excellent suppression of all overlapping ^{1}H resonances from PME and PDE. Discrimination of PC from GPE is obtained using selective ^{31}P refocusing either on PME or PDE (middle). As the chemical shifts of PME differ substantially from PDE in ^{31}P MRS, selectivity of the refocusing pulses is easily obtained (right). Therefore, individual PME and PDE metabolites can be selectively detected with POPE.

Conclusion and discussion

Although ^{1}H-^{1}H coupling generally degrades performances of polarization transfer sequences, in the POPE sequence with sLASER selection, the optimum TE for ^{1}H can be matched to that of ^{31}P. While the in vivo line width at 7T is dominated by unresolved J-coupling (^{31}P-^{1}H: 6-7 Hz) and intrinsic tissue inhomogeneities, the gain with POPE compared to direct ^{31}P MRS was still 2.8-fold in the human brain despite T2 losses. Consequently sensitivity enhanced detection of individual PME and PDE metabolites is feasible with ^{1}H MRS using ^{31}P editing as demonstrated in the human brain.

References *[1]. Katz-Brull et al. Cancer Res. 2002; [2]. van de Kemp et al. MRM 2011*